mice) as well as intestinal tissues of patients with appendicitis and IBD. Laser capture micro dissection and real time quantitative PCR has been applied to determine the mRNA expression of IL-2.

Results: Foxp3+ TR cells accumulate and proliferate in inflamed intestinal tissues. In experimental colitis, the number of contacts between Foxp3+ TR cells and proliferating Ki67+ (Foxp3-) cells significantly exceeded the theoretically expected random distribution. The accumulation of TR cells at proliferating cells is dependent on IL-2. Ki67+ proliferating cells express high level of IL-2 mRNA.

Conclusions: Proliferating IL-2 producing cells signal inflammation and provide Foxp3+ TR cells in the intestine with IL-2 that is in turn needed for TR maintenance and immunosuppressive activity.

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Permanent catalase activity impairment due to minor expression of catalase protein in peripheral white mononuclear cells of patients with naive and treated Crohn’s disease
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Background: Active Crohn disease (CD) patients have an increased oxidative stress, which depends on peripheral white mononuclear cells (PWMC) of active CD and decreased plasma antioxidants. We have previously shown increased reactive oxygen species peripheral leukocyte damage of active and inactive CD in order to clarify the origin of the oxidative stress damage and to study the correlation between activity and enzyme concentration.

Methods: Blood samples from healthy subjects (n=20, mean age 32±8) and from patients at first flare of CD, before initiating any specific medication and when been in remission (n=20, mean age 36.9±9.2) were obtained. Disease activity was scored with Harvey-Bradshaw index, and remission was defined as a disease activity index less than or equal to 4). PWMC were isolated by Ficoll-Bradshaw sedimentation. CAT activity was measured spectrophotometrically by enzymatic assays. Statistical analysis was performed with the Mann–Whitney test. CAT expression was studied in active CD patients, inactive CD patient and controls subjects by western blotting (WB) using anti-CAT monoclonal antibody.

Results: Harvey-Bradshaw index values were: Active CD (8.72±2.22), inactive CD (1±1.2). Inactive patients had the experiment performed when they were a mean time of 8.7±3 months in remission. CAT activity in PWMC of active and inactive CD is lower than healthy subjects (17.22±9.44 (p=0.0016 vs control) in active-CD and 10.38±4.47 (p=0.0003 vs control) in inactive CD and 33.51±15.9U/mg in controls. WB results have shown diminished levels of CAT in active and inactive CD patients than in control subjects (Figure 1).

Conclusions: CAT activity is inhibited in PWMC of active CD. This will help to the generation of H2O2 in the cells. The inhibition of CAT is permanent in CD as inactive-CD patients do not recover its activity. The results suggest a correlation between activity and CAT protein levels. This event could contribute to PWMC immunological functioning and thus could have an impact on the physiopathology of CD.

Reference(s)

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The stress mediators adenosine and hydrocortisone impair epithelial wound healing in vitro
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Introduction: Psychological stress worsens gut inflammation in inflammatory bowel disease (IBD). In some models, stress delays mucosal ulcer healing [1]. This process is initiated by restitution, the ingress of motile epithelial cells into the wound. The pro-inflammatory chemokine, interleukin (IL)-8, accelerates epithelial cell restitution [2].

Aims: To determine the effects of four putative neurohumoral mediators of the stress response on colonic epithelial cell restitution and IL-8 production in vitro.

Methods: Cell restitution velocity was measured over 24h in linear wounds made in confluent monolayers of human colon cancer-derived HT-29 cells. Cells were incubated with noradrenaline, adenosine, histamine and hydrocortisone in the presence and absence of fetal calf serum (FCS) (positive and negative control, respectively) and photomicrographs at 24h analysed with Digimizer software. For the IL-8 studies, HT-29 cells were pre-incubated with each stress mediator for 1h, then stimulated with IL-1β (1ng/ml). IL-8 in supernatants collected at 6h was assayed by ELISA. In each case n ≥ 4, and ANOVA was used to compare differences; restitution results for FCS are shown.

Results: Restitution velocity was dose-dependently inhibited by adenosine (10−6M: 3.3 (mean) ±0.42 (SD), p < 0.01; 10−5M: 2.4±0.31, p < 0.01; compared to relevant controls 4.9±0.21) and by hydrocortisone (10−4M: 4.8±0.75, p < 0.05; 10−5M: 4.4±0.66, p < 0.01 vs controls 6.0±0.73). Adenosine (10−5M: 327 pg/ml ±27, p < 0.01; 10−4M: 127±17, p < 0.01) and hydrocortisone (10−4M: 325±25, p < 0.01; 10−6M: 294±16, p < 0.01) each reduced IL-8 production compared to controls (449±30). At 10−9 and 10−7 M, neither noradrenaline nor histamine altered wound healing or IL-8 production.

Conclusions: These results suggest that psychological stress, by causing release of adenosine and hydrocortisone with subsequent reduction of epithelial IL-8 production, this could impair mucosal healing in IBD and perhaps other inflammatory diseases such as peptic ulcer. The adverse effects of hydrocortisone on epithelial restitution in vitro could also contribute to its failure to induce mucosal healing in Crohn’s disease.

Reference(s)